

**Effect of therapy on Quantiferon-Plus response in patients
with active and latent tuberculosis infection**

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keywords:

tuberculosis; latency; diagnosis; quantiferon; quantiferon plus

Supplementary Table S1: QFT-Plus results in LTBI subjects at the baseline and at the end of preventive therapy

QFT-Plus response to:	LTBI baseline (N. 46)	LTBI end of preventive therapy (N. 46)	Comparisons
	Positive N (%)	Positive N (%)	[#] <i>p</i>
either TB1 or TB2	46 (100)	40 (87)	0.03
TB1 and TB2	43 (93)	37 (80)	0.1
only TB1	1 (2)	1 (2)	1
only TB2	2 (4)	2 (4)	1
TB1	44 (96)	38 (83)	0.07
TB2	45 (98)	39 (85)	0.07

Footnotes: LTBI: latent tuberculosis infection; TB1: tube 1. TB2: tube 2; N:number.[#] Mc Nemar test

Supplementary Table S2: QFT-Plus results in LTBI subjects according preventive therapy used

QFT-Plus response to:	INH			INH and RIF		
	LTBI baseline (N. 32)	LTBI end of preventive therapy (N. 32)	Comparisons	LTBI baseline (N. 12)	LTBI end of preventive therapy (N. 12)	Comparisons
	Positive N (%)	Positive N (%)	[#] <i>p</i>	Positive N (%)	Positive N (%)	[#] <i>p</i>
either TB1 or TB2	32 (100)	27 (84)	<i>0.06</i>	12 (100)	11 (92)	<i>1</i>
TB1 and TB2	31 (97)	24 (75)	<i>0.02</i>	10 (83)	11 (92)	<i>1</i>
only TB1	0 (0)	1 (3)	<i>1</i>	1 (8)	0 (0)	<i>1</i>
only TB2	1 (3)	2 (6)	<i>1</i>	1 (8)	0 (0)	<i>1</i>
TB1	31 (97)	25 (78)	<i>0.03</i>	11 (92)	11 (92)	<i>1</i>
TB2	32 (100)	26 (81)	<i>0.03</i>	11 (92)	11 (92)	<i>1</i>

Footnotes: LTBI: latent tuberculosis infection; TB1: tube 1. TB2: tube 2; N:number. INH isoniazid. RIF rifampicine; [#] Mc Nemar test

Supplementary table S3: QFT-Plus results in LTBI subjects according the time of exposure to *M. tuberculosis*

QFT-Plus response to:	Recent			Remote		
	LTBI baseline (N.37)	LTBI end of preventive therapy (N.37)	Comparisons	LTBI Baseline (N.9)	LTBI end of preventive therapy (N.9)	Comparisons
	Positive N (%)	Positive N (%)	[#] <i>p</i>	Positive N (%)	Positive N (%)	[#] <i>p</i>
either TB1 or TB2	37 (100)	33 (89)	<i>0.1</i>	9 (100)	7(78)	<i>0.5</i>
TB1 and TB2	36 (97)	31 (84)	<i>0.1</i>	7(78)	6 (67)	<i>1</i>
only TB1	1 (3)	1 (3)	<i>1</i>	0 (0)	0 (0)	<i>n.a.</i>
only TB2	0 (0)	1 (3)	<i>1</i>	2 (22)	1 (11)	<i>1</i>
TB1	37 (100)	32 (86)	<i>0.06</i>	7 (78)	6 (67)	<i>1</i>
TB2	36 (97)	32 (86)	<i>0.2</i>	9 (100)	7 (78)	<i>0.5</i>

Footnotes: LTBI: latent tuberculosis infection; TB1: tube 1. TB2: tube 2; N:number; [#] Mc Nemar test; na: not applicable because the variable are not dichotomous

Supplementary table S4: QFT-Plus results in active TB patients at the baseline and at the end of therapy

QFT-Plus response to:	Active TB baseline (N. 28)	Active TB end of therapy (N. 28)	Comparisons
	Positive N (%)	Positive N (%)	[#]<i>p</i>
either TB1 or TB2	26 (93)	19 (68)	0.04
TB1 and TB2	25 (89)	19 (68)	0.07
only TB1	0(0)	0(0)	na
only TB2	1 (4)	0(0)	1
TB1	25 (89)	19 (68)	0.07
TB2	26 (93)	19 (68)	0.04

Footnotes: TB: tuberculosis; TB1: tube 1. TB2: tube 2; N:number; [#]Mc Nemar test; na: not applicable because the variable are not dichotomous

Supplementary table S5: QFT-Plus results in active TB patients according the microbiological results at the baseline and at the end of therapy

Active TB microbiologically confirmed				Active TB clinical diagnosis		
QFT-Plus response to:	Baseline (N. 19)	End of therapy (N. 19)	Comparisons	Baseline (N. 9)	End of therapy (N. 9)	Comparisons
	Positive N (%)	Positive N (%)	[#] <i>p</i>	Positive N (%)	Positive N (%)	[#] <i>p</i>
either TB1 or TB2	18 (95)	15 (79)	0.4	8 (89)	4 (44)	0.1
TB1 and TB2	17 (89)	15 (79)	0.6	8 (89)	4 (44)	0.1
only TB1	0 (0)	0 (0)	na	0 (0)	0 (0)	na
only TB2	1 (5)	0 (0)	1	0 (0)	0 (0)	na
TB1	17 (89)	15 (79)	0.6	8 (89)	4 (44)	0.1
TB2	18 (95)	15 (79)	0.4	8 (89)	4 (44)	0.1

Footnotes: TB: tuberculosis; TB1: tube 1; TB2: tube 2; N: number; [#]Mc Nemar test; na: not applicable because the variable are not dichotomous

Supplementary table S6: number of reversion according the definition of true reversion, uncertain reversion and manufacturing threshold.

	True reversion from IFN- γ values > 0.7 IU/mL to < 0.2 IU/mL		Uncertain reversion from IFN- γ values 0.2- 0.7 IU/mL to 0.2- 0.7 IU/mL or to <0.2 IU/ mL		Reversion according the package insert threshold from ≥ 0.35 IU/mL to <0.35 IU/mL	
	Number over total		Number over total		Number over total	
	LTBI	Active TB	LTBI	Active TB	LTBI	Active TB
TB1-peptides	6	5	1	3	8	9
TB2-peptides	2	5	2	3	7	9

Footnotes: TB: tuberculosis; TB1: tube 1; TB2: tube 2; N: number

Supplementary table S7: Similar distribution of IFN- γ values in response to peptides contained in TB1 and TB2 tubes, according the uncertain zone range in LTBI subjects.

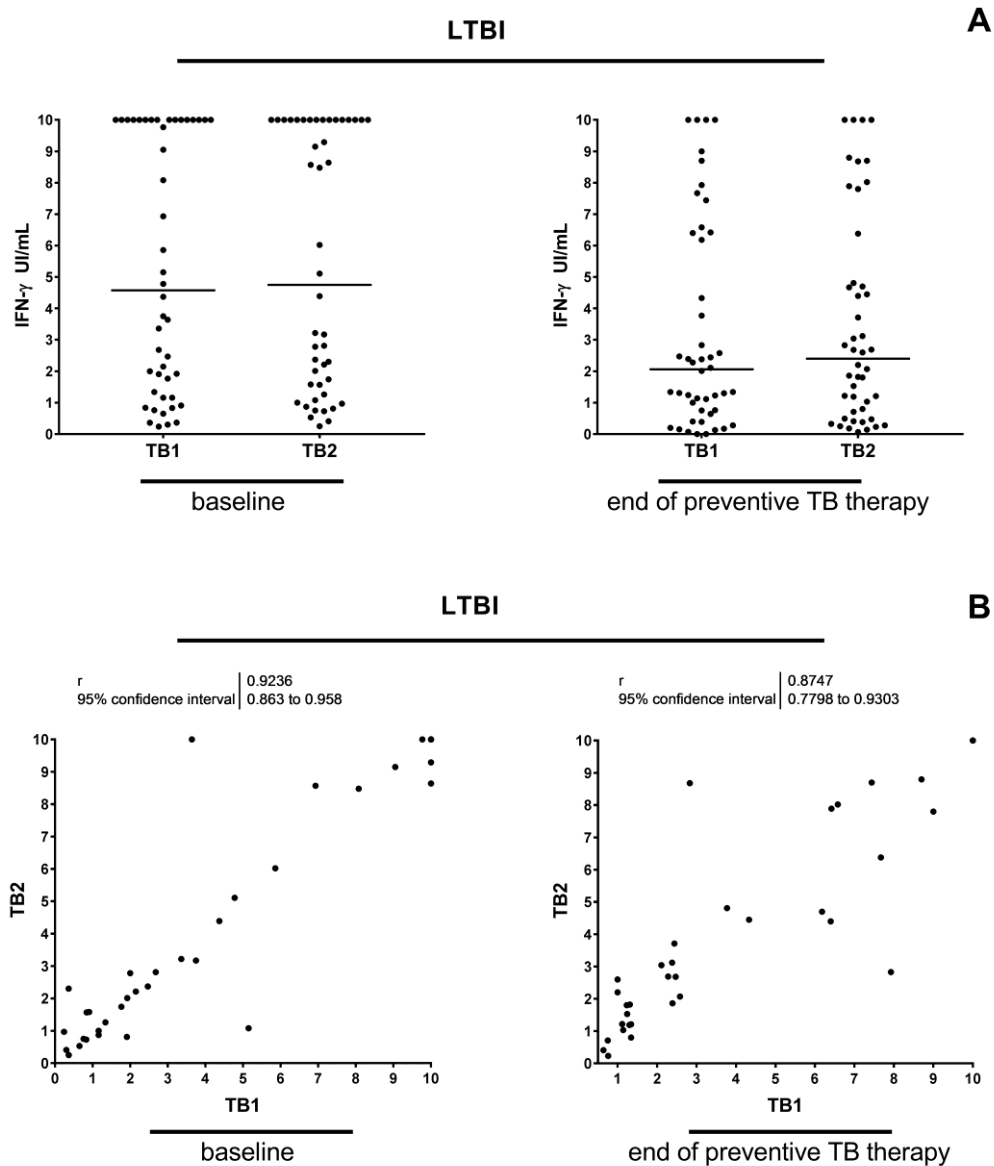
LTBI at the baseline		LTBI at the end of preventive therapy	
TB1-peptides stimulation range IFN- γ IU/mL (N)	Correspondent TB2-peptides stimulation range IFN- γ IU/mL (N)	TB1-peptides stimulation range IFN- γ IU/mL (N)	Correspondent TB2-peptides stimulation range IFN- γ IU/mL (N)
<0.2 (0)	/	<0.2 (6)	<0.2 (2) 0.2-0.34 (2) 0.35-0.7 (1) > 0.7 (1)
0.2-0.34 (2)	<0.2 (0) 0.2-0.34 (1) 0.35-0.7 (0) > 0.7 (1)	0.2-0.34 (2)	<0.2 (1) 0.2-0.34 (1) 0.35-0.7 (0) > 0.7 (0)
0.35-0.7 (3)	<0.2 (0) 0.2-0.34 (1) 0.35-0.7 (1) > 0.7 (1)	0.35-0.7 (3)	<0.2 (0) 0.2-0.34 (0) 0.35-0.7 (3) > 0.7 (0)
> 0.7 (41)	<0.2 (0) 0.2-0.34 (0) 0.35-0.7 (0) > 0.7 (41)	> 0.7 (35)	<0.2 (0) 0.2-0.34 (1) 0.35-0.7 (0) > 0.7 (34)

Footnotes: TB: tuberculosis; TB1: tube 1; TB2: tube 2; N: number

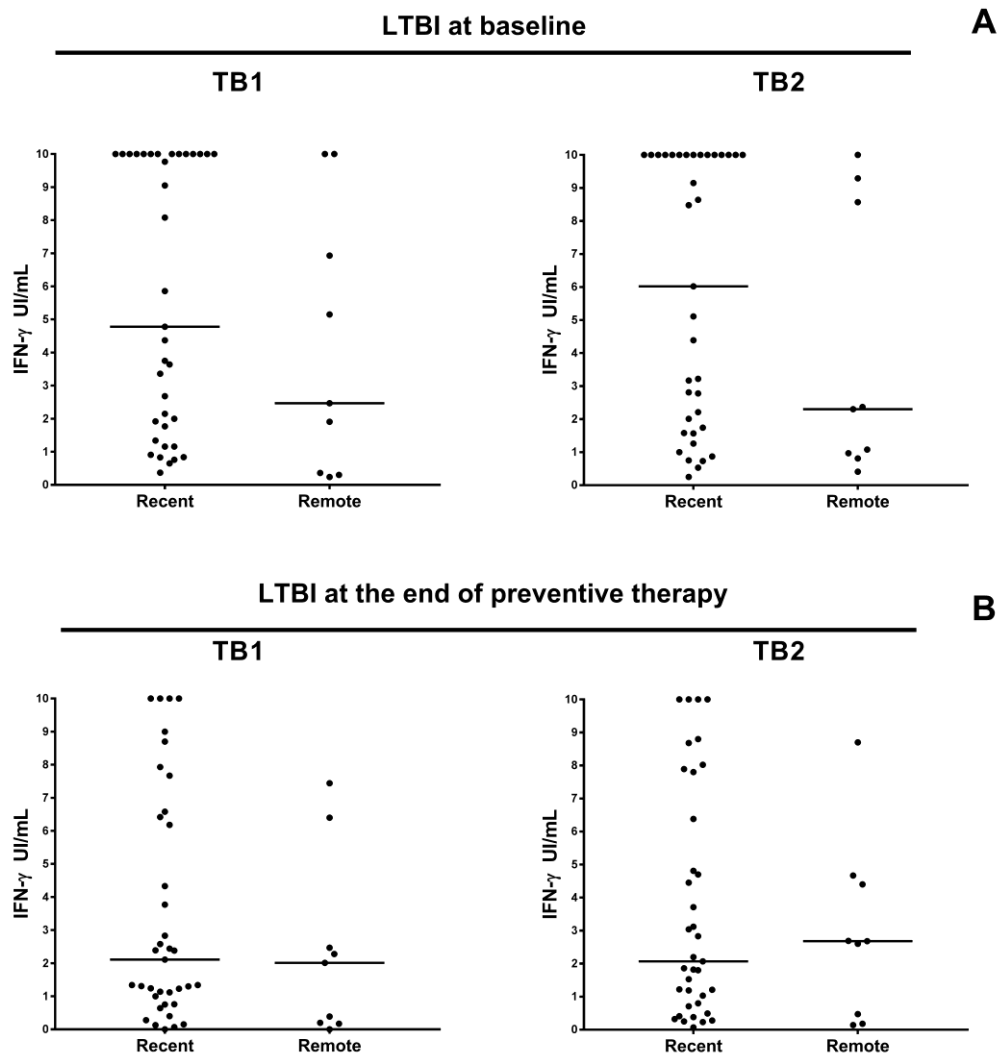
Supplementary table S8: Similar distribution of IFN- γ values in response to peptides contained in TB1 and TB2 tubes, according the uncertain zone range in active TB patients.

Active TB at the baseline		Active TB at the end of preventive therapy	
TB1-peptides stimulation range IFN- γ IU/mL (N)	Correspondent TB2-peptides stimulation range IFN- γ IU/mL (N)	TB1-peptides stimulation range IFN- γ IU/mL (N)	Correspondent TB2-peptides stimulation range IFN- γ IU/mL (N)
<0.2 (2)	<0.2 (2)	<0.2 (7)	<0.2 (7)
	0.2-0.34 (0)		0.2-0.34 (0)
	0.35-0.7 (0)		0.35-0.7 (0)
	> 0.7 (0)		> 0.7 (0)
0.2-0.34 (1)	<0.2 (0)	0.2-0.34 (2)	<0.2 (1)
	0.2-0.34 (0)		0.2-0.34 (1)
	0.35-0.7 (1)		0.35-0.7 (0)
	> 0.7 (0)		> 0.7 (0)
0.35-0.7 (3)	<0.2 (0)	0.35-0.7 (2)	<0.2 (0)
	0.2-0.34 (0)		0.2-0.34 (0)
	0.35-0.7 (3)		0.35-0.7 (1)
	> 0.7 (0)		> 0.7 (1)
> 0.7 (22)	<0.2 (0)	> 0.7 (17)	<0.2 (0)
	0.2-0.34 (0)		0.2-0.34 (0)
	0.35-0.7 (1)		0.35-0.7 (3)
	> 0.7 (21)		> 0.7 (14)

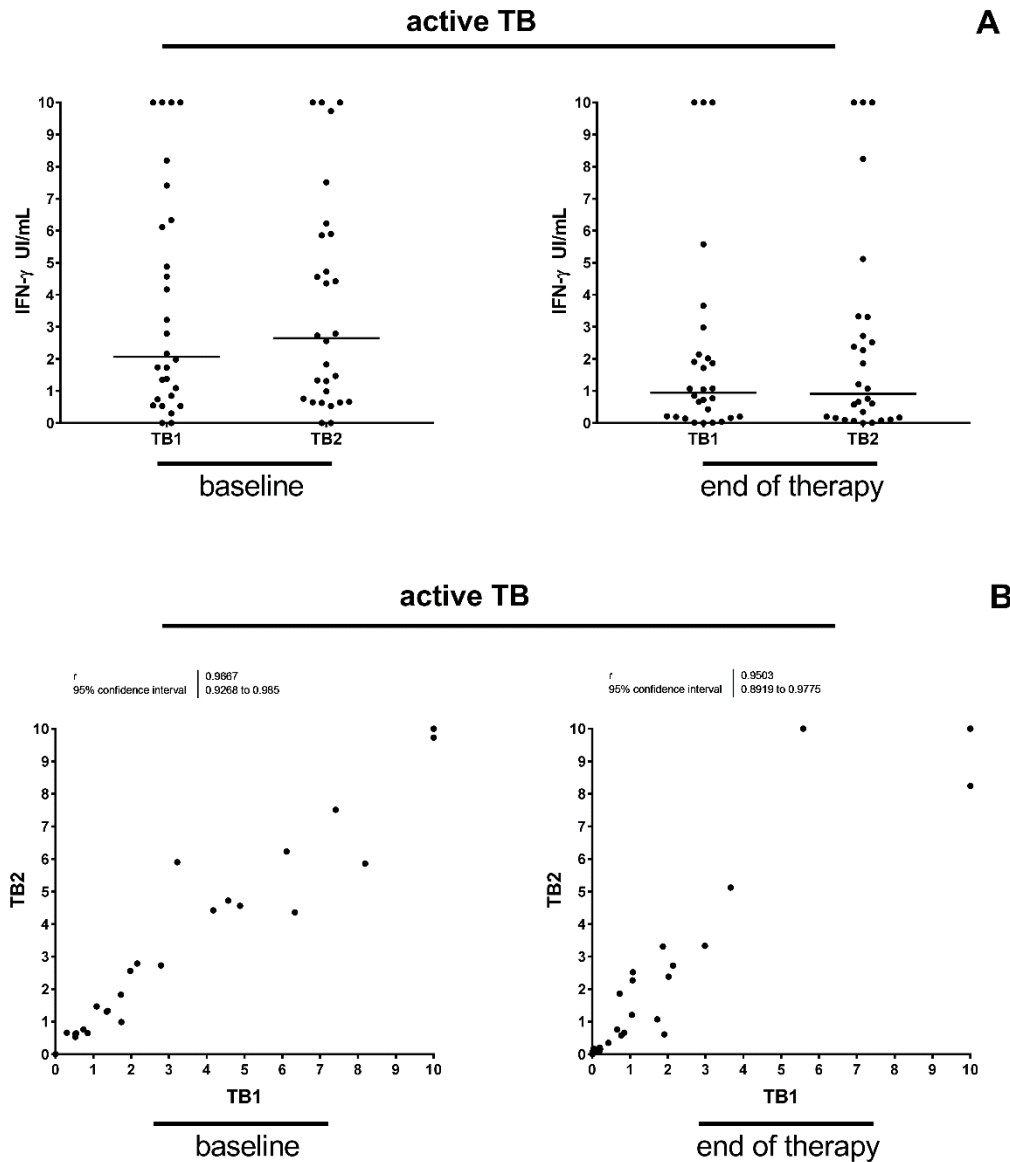
Footnotes: TB: tuberculosis; TB1: tube 1. TB2: tube 2; N: number



Supplementary figure S1: Comparison of IFN- γ response to antigens present in QFT-Plus test, TB1 and TB2, in LTBI subjects at the baseline and at the end of preventive therapy. A) IFN- γ response to TB1 and TB2 stimulation is similar both at baseline and at the end of preventive therapy. B) Positive correlation between the IFN- γ values in response to TB1 and TB2 stimulation both at baseline and at the end of preventive therapy. The data are presented as IU/mL. Mann–Whitney U test and Spearman correlation were performed. Footnotes: IFN: interferon; IU: international unit.



Supplementary figure S2: Comparison of IFN- γ response to QFT-Plus antigen TB1 and TB2 in recent and remote LTBI subjects at the baseline and at the end of preventive therapy. A) Recent and remote LTBI subjects at the baseline B) Recent and remote LTBI subjects at the end of preventive therapy. The data are presented as IU/mL, Mann–Whitney U test was performed. Footnotes: IFN: interferon; IU: international unit.



Supplementary figure S3: Comparison of IFN- γ response to QFT-Plus antigen TB1 and TB2 in active TB patients at the baseline and at the end of TB therapy. A) IFN- γ response to TB1 and TB2 stimulation is similar both at baseline and at the end of therapy; B) Positive correlation between the IFN- γ values in response to TB1 and TB2 stimulation both at baseline and at the end of therapy. The data are presented as IU/mL, Mann–Whitney U test and Spearman correlation were performed. Footnotes: IFN: interferon; IU: international unit.